UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,922	01/15/2002	Kari Alitalo	28967/37084A	3363

4743 7590 01/13/2005

MARSHALL, GERSTEIN & BORUN LLP
6300 SEARS TOWER
233 S. WACKER DRIVE
CHICAGO, IL 60606

EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/046,922	ALITALO ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 21-74* is/are pending in the application.

4a) Of the above claim(s) *39-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 21-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/26/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-13, and 21-74 are pending.

2. Claims 39-74 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. In view of the amendment filed 10/20/04, the following rejections remain.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 12, 21, and 22 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Y1 and Y2 in "Y1GYWLTIWGY2" of claim 12 are indefinite because the specification discloses Y1 and Y2 are cysteine residues only. One of ordinary skill in the art cannot appraise the metes and bounds of amino acids of Y1 and Y2.

The X1, X2, and X3 in "GYWX1X2X3W" of claim 21 is ambiguous and indefinite because specification discloses X1, X2 and X3 are L, T, I residues, respectively. One of ordinary skill in the art cannot appraise the metes and bounds of amino acids in X1, X2, and X3.

The X1, X2, X3 and X4 in "GYWX1X2X3WX4" in claim 22 is ambiguous and indefinite because specification discloses X1, X2 and X3 are L, T, I residues, respectively. One of ordinary skill in the art cannot appraise the metes and bounds of amino acids in X1, X2, X3 and X4.

Applicants' arguments filed 10/20/04 have been fully considered but are not found persuasive.

Applicants' position is that there is no restriction in the claim that these positions must be "particular" amino acids as the Examiner implies, and the terms should be interpreted as such, embracing, e.g. amino acids taught in the specification.

In response, the specification discloses only the specific amino acid substitution for the specific peptide GYWX1X2X3W (SEQ ID NO: 67) wherein X1, X2 and X3 are amino acids in the order selected from the group consisting of LTI (see page 27, line 25-27).

The Y1 and Y2 in "Y1GYWLTIWGY2" of claim 12 are indefinite because the specification discloses Y1 and Y2 are cysteine residues only. One of ordinary skill in the art cannot appraise the metes and bounds of amino acids of Y1 and Y2.

The X1, X2, and X3 in "GYWX1X2X3W" of claim 21 is ambiguous and indefinite because specification discloses X1, X2 and X3 are L, T, I residues, respectively. One of ordinary skill in the art cannot appraise the metes and bounds of amino acids in X1, X2, and X3.

The X1, X2, X3 and X4 in "GYWX1X2X3WX4" in claim 22 is ambiguous and indefinite because specification discloses X1, X2 and X3 are L, T, I residues, respectively. One of ordinary skill in the art cannot appraise the metes and bounds of amino acids in X1, X2, X3 and X4.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Hirohashi *et al* (Mol Pharmacol 53(6): 1068-75, June 1998 Jun; PTO 892).

Hirohashi *et al* teach an isolated peptide MLP-1 comprising the amino acid sequence ....GYWISWA...that is identical to the claimed peptide comprising the amino acid sequence GYWX1X2X3W (SEQ ID NO: 67) and GYWX1X2X3WX4 (SEQ ID NO: 68) wherein X1, X2, X3 and X4 are any amino acids (See Figure 3 (A) on page 1072, amino acid residues 964-974, in particular). The term "comprising" is open-ended. It expands the claimed peptide to include the reference peptide. Since the Patent Office does not have the facilities for examining and comparing the binding specificity of the claimed peptide to those of the prior art, the burden is on applicant to show that the prior art peptide is different from the claimed peptide. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 10/20/04 have been fully considered but are not found persuasive.

Applicants' position is that Hirohashi's protein has 1502 amino acids and has never been shown or suggested to bind VEGFR-3. The amended claims specify a peptide no larger than about 100 amino acids.

In response, the amended claims still recite "comprising" so long the peptide contains the amino acid sequence GYWX1X2X3W (SEQ ID NO: 67) and GYWX1X2X3WX4 (SEQ ID NO: 68) wherein X1, X2, X3 and X4 are any amino acids. Hirohashi *et al* teach an isolated peptide MLP-1 comprising the amino acid sequence ....GYWISWA...that is identical to the claimed peptide comprising the amino acid sequence GYWX1X2X3W (SEQ ID NO: 67) and GYWX1X2X3WX4 (SEQ ID NO: 68) wherein X1, X2, X3 and X4 are any amino acids (See Figure 3 (A) on page 1072, amino acid residues 964-974, in particular). The term "comprising" is open-ended. It expands the claimed peptide to include the reference peptide. Since the Patent Office does not have the facilities for examining and comparing the binding specificity of the claimed peptide to those of the prior art, the burden is on applicant to show that the prior art peptide is different from the claimed peptide. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirohashi *et al* (Mol Pharmacol 53(6): 1068-75, June 1998; PTO 892) in view of US Pat No 6,121,416 (Sept 2000; PTO 892).

The teachings of Hirohashi *et al* have been discussed supra.

The claimed invention as recited in claim 23 differs from the teachings of the reference only in that the isolated peptide further comprising amino- and carboxy-terminal cysteine residues.

The '416 patent teaches any peptide would have been conformationally stabilized by cyclization such as substituting at amino acids at the N and C terminal cysteines and is well known in the art that a disulfide bond can be formed between the terminal cysteines (See column 23, lines 28-67, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute or add a cysteine residue at both ends (amino- and carboxy-terminal cysteine residues) of a peptide taught by Hirohashi et al to form cyclization as taught by the '416 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to include cysteine residues at the amino- and carboxy-terminal of a peptide because disulfide bond can be formed between the terminal cysteines and cyclization via two terminal cysteines would have been expected to stabilized any peptides as taught by the '416 patent.

Applicants' arguments filed 10/20/04 have been fully considered but are not found persuasive.

Applicants' position is that Hirohashi's protein has 1502 amino acids and has never been shown or suggested to bind VEGFR-3. The amended claims specify a peptide no larger than about 100 amino acids.

In response, the amended claims still recite "comprising" so long the peptide contains the amino acid sequence GYWX1X2X3W (SEQ ID NO: 67) and GYWX1X2X3WX4 (SEQ ID NO: 68) wherein X1, X2, X3 and X4 are any amino acids. Hirohashi *et al* teach an isolated peptide MLP-1 comprising the amino acid sequence ....GYWISWA...that is identical to the claimed peptide comprising the amino acid sequence GYWX1X2X3W (SEQ ID NO: 67) and GYWX1X2X3WX4 (SEQ ID NO: 68) wherein X1, X2, X3 and X4 are any amino acids (See

Figure 3 (A) on page 1072, amino acid residues 964-974, in particular). The term "comprising" is open-ended. It expands the claimed peptide to include the reference peptide. Since the Patent Office does not have the facilities for examining and comparing the binding specificity of the claimed peptide to those of the prior art, the burden is on applicant to show that the prior art peptide is different from the claimed peptide. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

11. The following new ground of rejection is necessitated by the amendment filed 10/20/04.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-13 and 21-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for an isolated peptide consisting of the formula $X_1X_2X_3X_4X_5X_6X_7X_8$ wherein X1 is G, X2 is Y, X3 is W, X4 is L, X5 is T, X6 is I, X7 is W and X8 is G as set forth in SEQ ID NO: 35 wherein said peptide binds to VEGFR-3 and inhibiting the binding of VEGF-C from binding to VEGFR-3, the said peptide further comprises of amino and carboxy-terminal cysteine residues, a peptide dimer comprising a first and second peptide wherein the first and second peptide are SEQ ID NO: 35, a composition comprising the peptide consisting of an amino acid sequence of SEQ ID NO: 35 or a peptide dimer comprising a first and second peptide wherein the first and second peptide are SEQ ID NO: 35 and a pharmaceutically acceptable carrier for imaging or screening assay, **does not** reasonably provide enablement for (1) any isolated peptide "comprising" any amino acid sequence consisting of "8-100 amino acids comprising" the formula $X_1X_2X_3X_4X_5X_6X_7X_8$ (SEQ ID N0: 32) as set forth in claim 1, wherein X_1 through X_8 are any conservative amino acid substitution thereof and wherein the peptide comprises no more than 3 conservative amino acid substitutions introduced at position X_1 to X_8, (2) any isolated peptide "comprising" any amino acid sequence consisting of "8-100 amino acids comprising" the formula $CX_1X_2X_3X_4X_5X_6X_7X_8C$(SEQ ID N0: 33), wherein X_1 through X_8 are any amino acids, (3) all isolated peptide "comprising" any amino acid sequence consisting of "8-100 amino acids comprising" the sequence Y1GYWLTIWGY2 (SEQ ID NO: 34) wherein Y1 and Y2 are any amino acids, (4) all isolated peptide "comprising" any amino acid sequence consisting

of "8-100 amino acids "comprises" the sequence CGYWLTIWGC (SEQ ID NO: 35), (5) *any* isolated peptide comprising any amino acid sequence consisting of "7-100 amino acids comprising" the formula $GYWX_1X_2X_3W$ (SEQ ID NO: 67), wherein X1,X2 and X3 comprises any amino acids, and wherein the peptide binds VEGFR-3, (6) *any* isolated peptide comprising any amino acid sequence consisting of "7-100 amino acids comprising" the formula $GYWX_1X_2X_3WX_4$ (SEQ ID NO: 67), wherein $X_1X_2X_3$ and X_4comprises any amino acids, (7) the isolated peptides mentioned above further comprises amino carboxy-terminal cysteine residues, (8) the isolated peptides mentioned above further comprises an intramoleuclar bond between amino acid residues to form a cyclic peptide, (9) the isolated peptides mentioned above further comprises any cytotoxic agent, radioisotope, anti-neoplastic prodrug attached to said peptides, (10) any chimeric protein amino acid comprising any therapeutic protein amino acid sequence attached to the amino acid sequence of any peptide mentioned above, (11) any peptide dimer comprising any first and second peptide "comprising" any amino acid sequence consisting of "8-100 amino acids comprising" the formula $X_1X_2X_3X_4X_5X_6X_7X_8$ (SEQ ID N0: 32), wherein X_I through X_8 are any conservative amino acid substitution thereof and wherein the peptide comprises no more than 3 conservative amino acid substitutions introduced at position X_1 to X_8, or *any* isolated peptide comprising any amino acid sequence consisting of "7-100 amino acids comprising" the formula $GYWX_1X_2X_3WX_4$ (SEQ ID NO: 67), wherein X_1, X_2, X_3 and X_4 comprises any amino acids wherein the dimer binds to VEGFR3, and (12) any composition comprising any isolated peptide mentioned above for treating any cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a peptide consisting of the amino acid sequence GYWLTIWG of SEQ ID NO: 35 that binds to VEGFR-3 and inhibiting the binding of VEGF-C

from binding to VEGFR-3. The said peptide further comprises amino and carboxy terminal cysteine residues. The specification further discloses a peptide dimer comprising a first and second peptide wherein the first and second peptides are the same comprising SEQ ID NO: 35. A composition comprising said peptide or dimer and a pharmaceutically acceptable carrier for imaging or screening assays.

The specification does not teach how to make all isolated peptide mentioned above having an amino acid sequence consisting of 7 or 8-100 amino acids in addition to any combination of $X_1X_2X_3X_4X_5X_6X_7X_8$ because of the following reasons. First, the formula as recited in claim 1 has only 8 amino acids residues. Other than the specific 8 enumerated positions within the claimed peptide as disclosed on page 15, line 13-31, the rest of the amino acids within the claimed peptide such as 9, 10, 11, 12 ...98, 99 or 100 amino acids in length are not adequately enabled without the amino acid sequence. Second, the term "comprising", then "consisting", then "comprising" again is ambiguous. The peptide in claim 1 is treated as "comprising". The term "comprising" is open-ended. It expands the peptide to include additional amino acids at either or both ends. There is insufficient guidance as to which undisclosed amino acids to be added and whether the resulting peptide maintains its structure and function. Third, there is insufficient guidance as to which combination of $X_1X_2X_3X_4X_5X_6X_7X_8$ in peptide comprises no more than three conservative amino acid substitution and still maintain its structure and binding to VEGFR3. A peptide may bind to VEGFR-3 but it does not necessary means binding equal to inhibiting VEGF-C mediated function. Fourth, given the unlimited number of undisclosed peptide, there is insufficient working examples demonstrating that any peptide is effective for binding to VEGFR3, in turn, useful for treating cancer in vivo. Given the unlimited number of undisclosed peptide, it is unpredictable which undisclosed peptide having no more than 3 conservative in addition to having additional amino acids at either or both ends of the peptide would maintain its structure, let alone having competitive inhibition of VEGF-C/D binding to VEGFR-3. The specification discloses only peptide having no more than eight to ten amino acids residues in length as shown in the sequence listing, the rest of the claimed peptide as set forth in claims 1-13 and 21-38 without the amino acid has no structure, much less function.

With regard to claim 12, in addition to the problem with the sequence mentioned above, Y_1 and Y_2 encompass any amino acids. The specification discloses only cysteine for Y_1 and Y_2. Other than cysteine, there is insufficient guidance as to which amino acids in Y_1 and Y_2 and

whether any amino acids at Y_1 and/or Y_2 other than cysteine maintains the structure and binding specificity of the peptide to VEGFR3, in turn, effective for treating cancer in vivo.

With regard to claims 21-22, the claims encompass any amino acids at position $X_1X_2X_3$ in claim 21 and any amino acids at position X_1, X_2, X_3 and X_4 in claim 22. The specification discloses only amino acids at $X_1X_2X_3$ are LTI, respectively. There is insufficient guidance as to the other amino acids at position $X_1X_2X_3$ in claim 21 and $X_1X_2X_3$ and X_4 in claim 22 that would maintain the structure and function as the peptide that binds to VEGFR-3, in turn, effective as a pharmaceutical for treating cancer. Further, the term "comprising" is open-ended. It expands the peptide of SEQ ID NO: 67 or SEQ ID NO: 68 to include additional amino acids at either or both ends so long the peptide consisting of 7-100 amino acids in length. Since SEQ ID NO: 67 and SEQ ID NO: 68 are merely 7 or 8 amino acids in length, respectively, the rest of the amino acids within the claimed peptide such as 9, 10, 11, 12 ...98, 99 or 100 amino acids in length are not adequately enabled without the amino acid sequence.

With regard to claim 30, in addition to the problem of undisclosed peptide mentioned above, there is insufficient guidance as to the "therapeutic protein amino acid sequence" without the amino acid sequence. Without the amino acid sequence, one of skilled in the art cannot make, much less use the claimed invention.

With regard to claim 31, in addition to the problem of undisclosed peptide and therapeutic protein amino acid sequence mentioned above, the chimeric protein now "comprises" a tumor necrosis factor. Since the peptides in claims 1 and 21 mentioned above are not enabled, it follows that the chimeric protein comprising said undisclosed peptide and tumor necrosis factor is not enabled.

With regard to claim 32, there is insufficient guidance as to the binding specificity of all antibody or fragment thereof. Since the peptides in claims 1 and 21 mentioned above are not enabled, it follows that the undisclosed peptide attached to any antibody or fragment thereof is not enabled. The same reasons apply to peptide dimmers as set forth in claims 34-37. It also follows that the composition comprising any peptide in claim 1 and 21 are not enabled.

With regard to claim 33, in addition to the problem with the peptide in claims 1 and 21 mentioned above, there is insufficient guidance as to which particular "modification" that would increase the circulating in-vivo half-life of said undisclosed peptide. The same reasons apply to peptide dimmers as set forth in claims 34-37.

Stryer *et al*, of record, teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions could result in substantially different pharmacological activities.

Attwood *et al*, of record, teaches that protein function is context-dependent; the state of the art of making functional assignments merely on the basis of some degree of similarity between sequences and the current structure prediction methods is unreliable and knowing structure alone will not inherently tell us function (See figure, entire document).

Given the lack of amino acid sequences for all undisclosed peptide, it follows that any undisclosed peptide further comprises amino and carboxyl terminal cysteine residues are not enabled. It also follows that any undisclosed peptide that forms intramolecular bond or disulfide bonds between cysteine residues are not enabled. It stands to reason that any cytotoxic agent, radioisotope, anti-neoplastic prodrug, chimeric protein, composition and dimer comprising the undisclosed peptide are not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 10/20/04 have been fully considered but are not found persuasive.

Applicants' position is that the specification, at page 14, line 14, to page 17, line 18, describes the peptides contemplated by the invention, including the specific conservative amino acid substitutions contemplated. Moreover, the specification at page 35, line 8, to page 38, line 6, teaches methods for making peptides using techniques common in the art such as solid phase synthesis, preparation from a phage library, and recombinant expression systems.

In contrast to applicant's assertion that the specification teaches peptides contemplated by the invention, the specification discloses only a peptide consisting of the amino acid sequence GYWLTIWG of SEQ ID NO: 35 that binds to VEGFR-3 and inhibiting the binding of VEGF-C from binding to VEGFR-3. The said peptide further comprises amino and carboxy terminal cysteine residues. The specification further discloses a peptide dimer comprising a first and second peptide wherein the first and second peptides are the same comprising SEQ ID NO: 35. A composition comprising said peptide or dimer and a pharmaceutically acceptable carrier for imaging or screening assays. None of the peptides disclosed in specification are more than 10, 11, ...98, 99 or 100 amino acids in length (see page 16-17 of specification). A peptide without the amino acid sequence has no structure, much less function. Without the amino acid sequence, one of skill in the art cannot make, i.e. solid phase synthesis, recombinant expression system, much less use the claimed peptide. Although the specification discloses a method of screening or preparing from a phase library, it is not routine to screen peptide having a length such as 97, 98 99 or 100 amino acids in length. Until the peptide has been identified, the specification as filed merely extended an invention to one skilled in the art to come up with the structure the claimed peptide look like without the amino acid sequence. Applicant is directed to the detailed explanation above.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

17. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
January 7, 2005

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600